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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,814	07/05/2001	Francisco Javier Garcia-Ladona	0480/001210	1323

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EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/869,814	GARCIA-LADONA, FRANCISCO JAVIER	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-35* is/are pending in the application.

4a) Of the above claim(s) *19-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *29-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *19-35* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED OFFICE ACTION

Applicant's amendment in paper No. 5, filed on 08 November 2002 is acknowledged and entered. Following the amendment, the original claims 1-18 are canceled, and the new claims 19-35 are added.

In view of the current condition of the claims, which embrace more than one patentably distinct invention, a restriction requirement is imposed.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 19-28, drawn to a screening process for identification of compounds, classified in class 435, subclass 7.1.

II. Claims 29-35, drawn to a method of treatment using 5-HT5 receptor ligand, classification depending upon the chemical entity of the ligand.

Applicant's election with traverse of the invention represented by claims 29-35, in Paper No. 7, at page 3, filed on 07 February 2003, is acknowledged.

Applicants clarify that the original restriction requirement was based on the original claims 1-18, which were not pursued in the present national stage prosecution, and that the intended claims 1-17, which were not entered, were reintroduced as new claims 19-35. As such, currently; only claims 19-35 are pending. Further, Applicants indicate that the original Group I included claims (claims 10-12) drawn to a process for using the binding partners to treat cerebrovascular diseases, which are represented by current pending claims 29-35.

With respect to the traversal, it is on the ground(s) that the two processes share a specific technical feature in that each involves the isolation *or* use of compounds, which selectively bind to 5-HT5 receptor. This is not found persuasive because the two processes do not share a specific technical feature for the following reasons: the process for identifying a compound is neither a process of making, nor a process of using the compound, whereas the method of treatment is a process of using the compound, thus, there is no specific technical feature link the two processes. Further, each of the processes has different method steps, different active agents, different starting and ending points, and is for a completely different purpose, such that they do not share a specific technical feature.

The requirement is still deemed proper and is therefore made FINAL.

Currently, claims 19-35 are pending, and claims 29-35 are under consideration. Claims 19-28 are withdrawn from further consideration as being drawn to a non-elected invention.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are directed.

The specification is objected to for the following informalities, appropriate correction is required for each item:

At page 3, line 41, the sentence is not complete as it starts with "or include ...".

Objections and Rejections under 35 U.S.C. 112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29-35 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 is indefinite because it is unclear what "an effective amount" is for, as the preamble merely recites "a method for treating *cerebrovascular disorders*". It is unclear for what effect specifically the amount is effective for.

Claim 30 is indefinite for the recitation of "by at least *the factor 2*". It is unclear whether "the factor 2" means n x 2, n^2, or something else. The metes and bounds of the claim, therefore, cannot be determined. Claim 31 is similarly indefinite.

Claim 35 is indefinite because it is unclear what "the *acute* treatment of migraine" is meant, and what is the difference between "the treatment of migraine" in claim 34 and "the *acute* treatment of migraine" in the instant claim.

The remaining claims are rejected for depending from an indefinite claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 29-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 29-35 are directed to a method for treating cerebrovascular disorders such as migraine with binding partners for 5-HT5 receptor. However, the specification provides no guidance, nor working example to support such use. Working examples in the specification are noted, however, they are merely in vitro binding assays and signal transduction assays, which, by no means, are the indications of effectiveness for in vivo treatment. [Although the prior art has established that certain disorders such as migraine may be treated with 5-HT receptor ligands that bind to certain specific 5-HT receptors such as 5-HT1D, one may not automatically deduce from such that a binding partner for other 5-HT receptors such as 5-HT5 would be suitable for the same treatment because each 5-HT receptor has different expression pattern, which determines the functional difference. As such, one of skilled in the art would not accept that binding partners for 5-HT5 receptor would be beneficial to those individuals having cerebrovascular disorders without any evidence link to effectiveness of such treatment. A search of the prior art reveals that there are 13 or more subtypes of 5-HT receptors, and they have distinct expression patterns with some overlaps. As such, they may display different functional properties depending upon their tissue distribution. For instance, Borne, in his review article (Drug Topics 1994, 138, 108-117), teaches that 5-HT1D is the most abundant 5-HT1 receptor in the CNS but is also found in vascular smooth muscle mediating contraction (page 110, the right

column),, that migraine represents a disorder of cerebral vascular regulation and may be the result of a marked, prolonged phase of cranial vasodilation (page 112, the right column), that serotonin is released during migraine attacks, and the major metabolite of 5-HT, 5-hydroxyindoleacetic acid (5-HIAA), is excreted in increased amounts, of all the 5-HT receptors, the 5-HT1 subtype has been most widely implicated, since these receptors are mainly located in certain cranial blood vessels (the paragraph bridging pages 112-113). Further, Prusinski (Neurol. Neurochir. Pol., 1992, Suppl., 2: 28-48) teaches that Sumatriptan, an agonist of 5-HT1 like receptor and effective in abortion of migraine attacks, exerts a selective vasoconstricting effect on the arteries of the head (the abstract). Additionally, Carson et al. (GLIOA No.17 :317-326, 1996, provided by applicants) teaches that the primary site of expression of 5-HT5A receptors is non-neuronal astrocytes (the abstract, and page 319, the right column). Therefore, given the facts that migraine is associated with cranial vasodilation, and 5-HT5 is not expressed in cranial blood vessels as 5-HT1D is, that the prior art has not established that migraine is associated with astrocytes in any way, and that the instant specification does not provide any evidence to support otherwise, the claimed method of treating migraine or any other cerebrovascular disorder is not enabled, and, undue experimentation is required to determine such.

Due to the large quantity of experimentation necessary to determine whether a binding partner for 5-HT5 receptor is suitable for the treatment of migraine or any other cerebrovascular disorder, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art, which has not established that astrocytes are associated with migraine or other cerebrovascular disorders, undue experimentation would be required of the skilled artisan to use the claimed invention.

Prior Art:

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Carson et al. (GLIOA No.17 :317-326, 1996, provided by applicants) discloses that the 5-HT5A is expressed predominantly by astrocytes (the abstract, and page 319, the right column).

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
5/8/03